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RHODIUM CATALYZED DIRECT COUPLING OF α,β-UNSATURATED KETONE, ALDEHYDE, AND TRIALKYLSILANE: AN EASY ACCESS TO REGIO-DEFINED ALDOL DERIVATIVES

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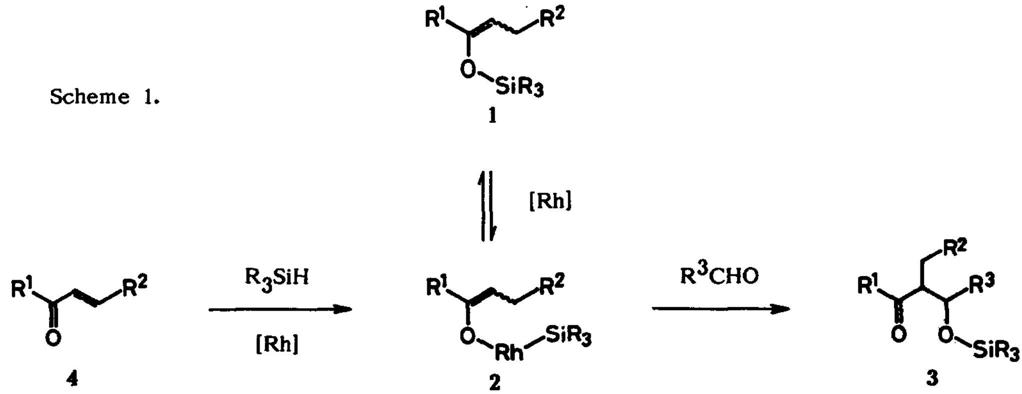
Summary: Regio-defined aldol type compounds are successfully formed by a one-pot reaction of α, β-unsaturated ketones, aldehydes, and Et_2MeSiH with the aid of a catalytic amount of $Rh_4(CO)_{12}$ or $Rh_4(CO)_{12}/MePh_2P$ under almost neutral conditions.

We have recently shown that $Rh_4(CO)_{12}$ and $[Rh(COD)(DPPB)]X$ ($X=PF_6$ and ClO_4) are effective as promoters for aldol couplings of enol trimethylsilyl ethers (**1**) with aldehydes or ketones under neutral conditions.[1, 2] We pointed out putatively that an intermediate like **2** plays an important role in that reaction. The existence of such a complex is proved by the isolation of the O-bound rhodium enolate complex which reacts with benzaldehyde to give rhodium aldolate complex.[3] On the other hand, it is also well known that Rh(I) complexes catalyze the hydrosilylation of α, β-unsaturated ketones to give **1**.[4] Detailed mechanistic consideration aside, an introduction of rhodium enolate **2** is convenient for the consistent elucidation of the role of rhodium metal. Thus, these two different reactions (**1** → **3** and **4** → **1**) can be amalgamated to each other through the intervention of **2**. This analysis sheds light on the direct synthesis of aldol type compounds from α,β-unsaturated ketone, trialkylsilane, and aldehyde (Scheme 1). We report here a successful coupling of these substrates in one-pot reaction with the aid of $Rh_4(CO)_{12}$ or a combination of $Rh_4(CO)_{12}$ and phosphine ligands.

When the reaction of an equivalent of each of 3-buten-2-one (**4a**), PhCHO, and Et_2MeSiH was carried out with a catalytic amount of $Rh_4(CO)_{12}$ in benzene at ambient temperature, aldol

Scheme 1.



type product **5a** was isolated in 21 % yield after the chromatographic purification of the mixture and subsequent bulb-to-bulb distillation. An appreciable amount of **1a** was detected along with the formation of **5a** by gas chromatographic analysis of the reaction mixture. In fact, $Rh_4(CO)_{12}$ also efficiently catalyzes the respective reactions of Et_2MeSiH with **4a** to form enol silyl ether **1a** and with PhCHO to form benzyloxysilane under analogous conditions. Despite the poor yield of **5a** (syn:anti = 80:20), it is interesting that this simple operation makes possible the aldol type coupling among the three components. $Rh_4(CO)_{12}$ cannot catalyze the crossed aldol reaction of preformed **1** with aldehydes at ambient temperature.[1] Therefore, the formation of **1a** and **5a** seems to be competitive aspect of this three component coupling. The yield of **5a** was enhanced remarkably by the presence of an excess of both **4a** and Et_2MeSiH (**4a**:Et_2MeSiH:PhCHO = 4:2:1), in addition to conduct of the operation at below room temperature to suppress the formation of **1a**. It is interesting that homocoupling products[6] of **4a** were not detected at all under the conditions used, even in the presence of an excess of **4a** and rhodium complex. The results are summarized in Table 1, in which it is shown that hexane or toluene is the choice of solvents and -15 °C is the lowest temperature allowing the coupling reaction to proceed. $Rh_4(CO)_{12}$ is far more effective as a catalyst precursor than

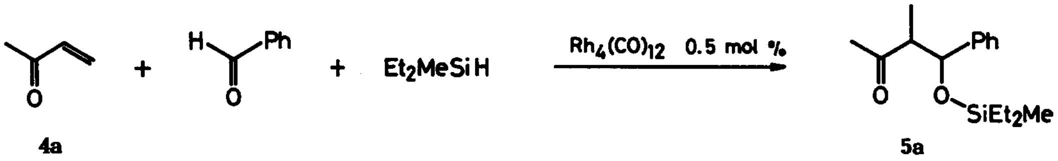


Table 1. $Rh_4(CO)_{12}$ catalyzed three component coupling of **4a**, PhCHO, and Et_2MeSiH.[a]

Entry	Conditions		Aldol product **5a**	
	Solvent	°C/h	Yield(%)[b]	syn:anti[c]
1	None	20/1	42	50:50
2	Hexane	20/15	97	77:23
3	Hexane	0/3	95	86:14
4	Hexane	-15/3	85	88:12
5	Benzene	20/1	64	81:19
6	Toluene	-15/7	98	87:13
7	CH_2Cl_2	-15/9	93	85:15
8	THF	-15/5	53	78:22

[a] Reactions were conducted on a scale of 2 mmoles with respect to PhCHO.

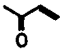
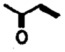
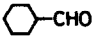
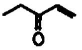
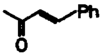
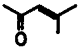
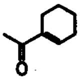
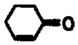
[b] Isolated yield.

[c] The ratio was determined by capillary GLC analyses (PEG-HT Bonded, 25 m column).

the other types of complex, $RhCl_3 \cdot 3H_2O$,[7a] $Co(DPM)_2$,[7b] $RhH(PPh_3)_4$, $RhCl(PPh_3)_4$, or $[Rh(COD)(DPPB)]X$ ($X = PF_6$ or ClO_4) in the present reaction.

In contrast to the success of PhCHO, the present three component coupling did not provide acceptable results for enolizable aldehydes under similar conditions. The problem, however, is surmounted by the modification of $Rh_4(CO)_{12}$ with $MePh_2P$. The yield of an aldol

Table 2. Three components coupling catalyzed by phosphine modified $Rh_4(CO)_{12}$.[a]

				Conditions		Product	
Entry	α,β-Enone	Aldehyde	Phosphine[b]	Solvent	°C/h	Yield (%)[c]	syn:anti[d]
1		PhCHO	$MePh_2P$	Toluene	-5/2	99	83:17
2		Hexanal	None	Hexane	-15/7	42	71:29
3		Hexanal	$MePh_2P$	Hexane	15/2	80	68:32
4			None	Hexane	15/5	22	60:40
5			$MePh_2P$	C_6H_6	20/3	63[e]	58:42
6			Ph_3P	C_6H_6	20/2.5	45[e]	60:40
7			Bu_3P	C_6H_6	20/2	49[e]	58:42
8			DPPB	C_6H_6	20/2	53[e]	57:43
9			DCPE	C_6H_6	20/3.5	59[e]	60:40
10		Hexanal	None	Hexane	0/6.5	21	73:27
11		Hexanal	$MePh_2P$	Hexane	15/6	45	74:26
12		PhCHO	$MePh_2P$	Hexane	0/20	100	84:16
13		PhCHO	$MePh_2P$	C_6H_6	20/3.5	88	55:45
14		PhCHO	None	C_6H_6	20/7	0	--
15		PhCHO	$MePh_2P$	C_6H_6	20/7	86	80:20
16		PhCHO	$MePh_2P$	C_6H_6	20/15	69	--
17		PhCHO	None	Toluene	15/15	57	75:25
18		PhCHO	$MePh_2P$	Toluene	0/5	75	73:27

[a] Reactions were conducted on a scale of 2 mmoles with respect to an aldehyde.

[b] DPPB: 1, 4-Bis(diphenylphosphino)butane, DCPE: 1, 2-Bis(dicyclohexylphosphino)ethane.

[c] Isolated yield.

[d] The ratio was determined by capillary GLC analyses (PEG-HT Bonded, 25 m column).

[e] Isolated as the aldol derivatives after the protodesilylation of **5**.

type product was improved remarkably when the coupling reaction was carried out in this catalyst solution which was prepared in situ by mixing $Rh_4(CO)_{12}$ and two equivalents of $MePh_2P$ in an adequate solvent at ambient temperature. The phosphine modified catalyst is effective for the coupling of enolizable aldehydes. The results of cyclohexanecarboxaldehyde show that $MePh_2P$ is the choice of ligands. A dramatic effect of the presence of $MePh_2P$ was also observed in the reaction of 4-methyl-3-penten-2-one with PhCHO. However, this modification of catalyst was not effective for the coupling of a β-substituted **4** with an enolizable aldehyde. The results are summarized in Table 2. It shows that this method provides a facile regio-defined route to aldol derivatives without base or acid in spite of some limitations.

The intervention of **2** is one plausible explanation of the present coupling reaction, although no direct information about the existence of **2** was obtained from the ^1H NMR observation of a stoichiometric mixture of $Rh_4(CO)_{12}$, **4a**, and Et_2MeSiH. It is interesting that the coupling reaction is applicable to enolizable aldehydes at relatively low temperature in contrast to the previous report.[3] CO ligands of $Rh_4(CO)_{12}$ are readily substituted by phosphines to give tetra-nuclear complexes[8], therefore, it is surmised that the tetra-nuclear structure of the catalyst can be retained intact regardless of the presence or absence of $MePh_2P$ in the catalyst solution. The cluster frame of rhodium metals may play an important role in our catalytic coupling. Further studies are now in progress.

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   (b) T. Hayashi, K. Yamamoto, and M. Kumada, Tetrahedron Lett., 3 (1975).
5. These products are identified by IR and ^1H NMR spectra and combustion analyses. Diastereo isomers are determined by comparison of the IR and ^1H NMR spectra of the protodesilylated products of each isomer with the literature or authentic samples.
6. (a) S. Sato, I. Matsuda, and Y. Izumi, Chem. Lett., 1875 (1985). (b) S. Sato, I. Matsuda, and M. Shibata, J. Organomet. Chem., **377**, 347 (1989).
7. $RhCl_3 \cdot 3H_2O$ and $Co(DPM)_2$ are effective for the coupling among α,β-unsaturated ester or amide, aldehyde, and silane; however, neither is effective for the reaction of **4a**.
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